Design of a Dielectrophoretic Based Micropipette for Gene Expression Applications Using COMSOL Multiphysics®

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Introduction: COMSOL Multiphysics® was used to design a dielectrophoresis (DEP) based micropipette for single-cell gene expression profiling.

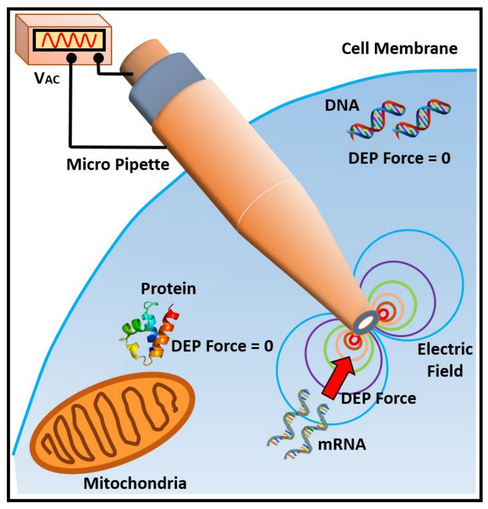


Figure 1: Schematic representation of DEP based single-cell mRNA extraction technique (not to scale).

The designed micropipette consists of an electrode inside and one electrode outside of the surface. In experiments, it is inserted into single cells to extract mRNA (representative of genes) through DEP.

As DEP depends on Electric Field ($\boldsymbol{E}$) and its gradient (∇E^2) , we used COMSOL calculations to calculate variations of $\boldsymbol{E}$ and (∇E^2) at the vicinity of the micropipette.

Computational Methods:

1. Geometry : Two dimensional axis-symmetric model from COMSOL was used to model the micropipette that is penetrated into a cell. The geometry was densely meshed into finite elements for calculations.

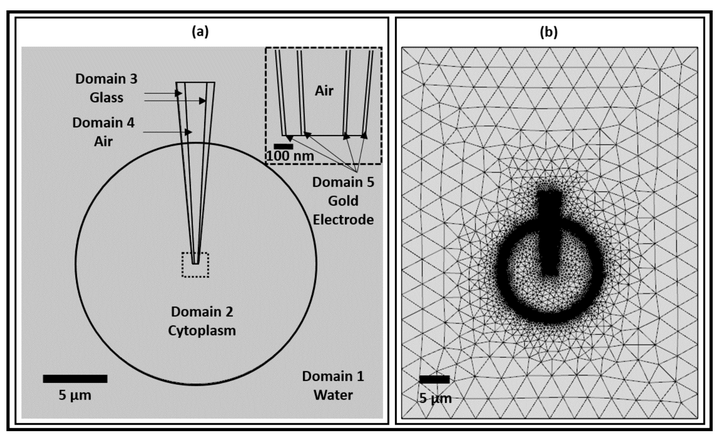


Figure 2. (a) The geometry of the model; inset provides details at the apex of the micropipette. (b) User defined highly dense mesh of the system

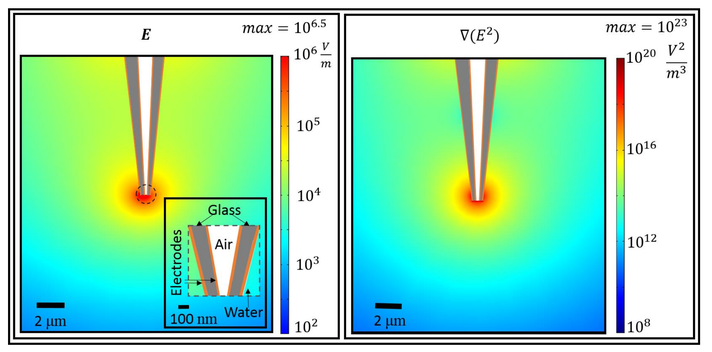
2. Physics and Governing Equations: AC/DC module of COMSOL Multiphysics ® was utilized in calculations.

- **DEP** : As DEP force $\boldsymbol{F_{DEP}} \propto (\boldsymbol{\nabla E^2})$, $\boldsymbol{E}$ and (∇E^2) was calculated by a frequency domain analysis at 120kHz.
- **Capture Volume:** Capture volume is the region in which DEP is large enough to attract molecules towards the micropipette tip. It is defined as,

  $\frac{1}{2}\boldsymbol{\alpha E^2} \geq \boldsymbol{KT}$; α – Polarizability of molecules

  $\boldsymbol{K}$- Boltzamann Costant, $\boldsymbol{T}$- Absolute Temperature.

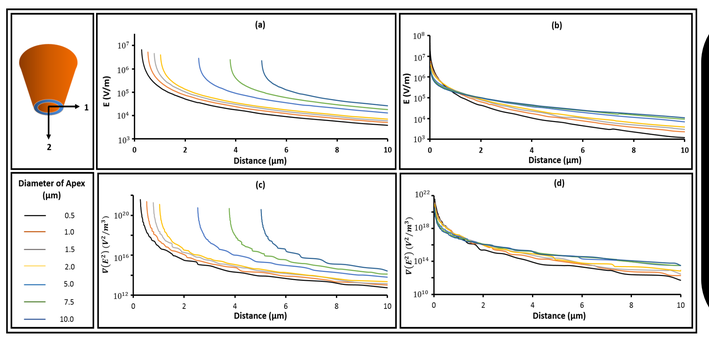
Results: We have calculated $\boldsymbol{E}$ and ∇E^2 in the vicinity of the micropipette assuming that it is inserted into a cell.



This is the highest ∇E^2 ever reported. A higher ∇E^2 will ensure a high-throughput mRNA extraction.

Figure 3. Calculated E and ∇E^2 near the micropipette tip

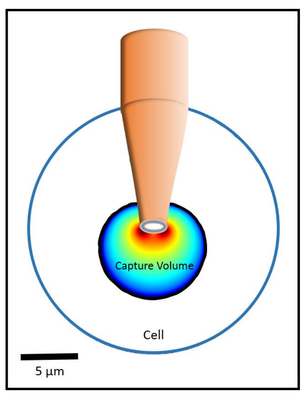
We optimized the diameter of the micropipette in order to have a high DEP at the micropipette tip.



A diameter of 0.5- 2.0 µm for the micropipette tip can be effectively used to extract molecules.

Figure 4. Variation of E and ∇E^2 with the diameter of the micropipette

Also, We calculated the capture volume of the system.



The calculated capture volume is about 22% of the total cytosol volume.

Figure 5. Calculated capture volume

Conclusions: We have successfully utilized AC/DC module to calculate E and $\nabla(E^2)$ near the tip of a micropipette with fabricated electrodes. We have also calculated the capture volume of the micropipette. Currently, experiments are being performed to find other important parameters such as range, throughput and sensitivity.

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